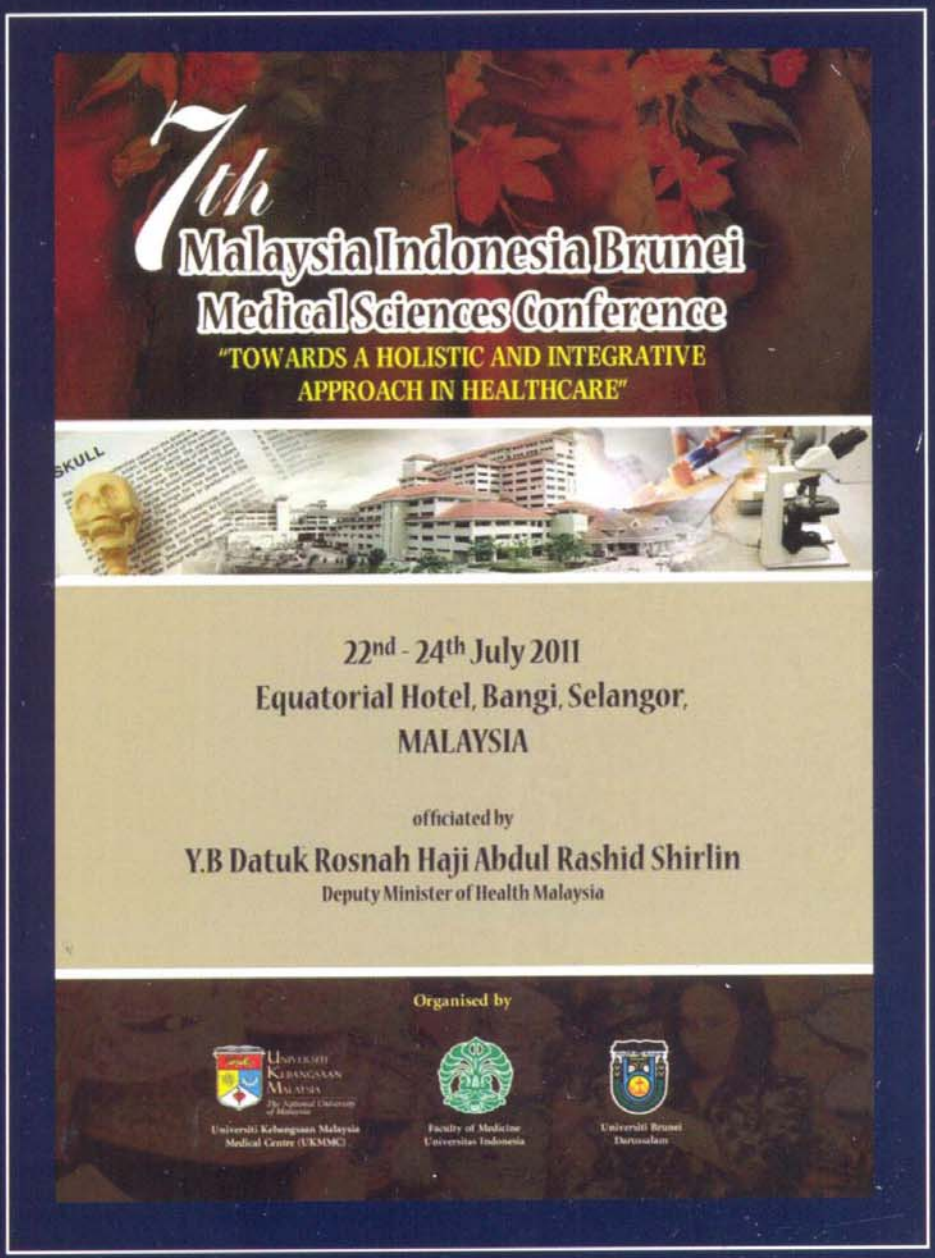
Volume 6, No. 1 (Supplement)
June 2011
ISSN 1823-2140

The National University with an INTERNATIONAL REACH

UNIVERSITI KEBANGSAAN MALAYSIA
National University of Malaysia

MEDICINE & Health

The Official Journal of The Faculty of Medicine UKM



MODULATION OF SENESCENCE ASSOCIATED GENES EXPRESSION IN HUMAN DIPLOID FIBROBLASTS BY TOCOTRIENOL-RICH FRACTION PREVENTS CELLULAR SENESCENCE

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Background:
Human diploid fibroblasts (HDFs) have a limited ability to divide when cultured *in vitro* and eventually enter a state of irreversible proliferation, termed replicative or cellular senescence. This study was conducted to evaluate the anti aging effects of tocotrienol-rich fraction (TRF) by determining the expression of senescence associated genes in human diploid fibroblasts (HDFs).

Materials and Methods:
Primary HDFs were cultured into passage 4 (young cells), passage 15 (pre-senescent cells) and passage 30 (senescent cells) with and without TRF treatment. Expression of antioxidant associated genes (*SOD1, SOD2, CAT, GPx-1, CCS-1, AOP-2*), IGF-1/ PI3K/ Akt associated genes (*FOXO3a*), DNA damage ($p16^{INK}$, $p21^{WAF}$, *p53*) and cell proliferation genes ($p38^{MAPK}$, *AP-1*) was quantitatively analyzed with real time RT-PCR method.

Results:
Expression of *p53* and $p21^{WAF}$ was increased in senescent HDFs. Similar increase in gene expression was observed in senescent HDFs for *AOP-2* and $p38^{MAPK}$ with no change in *FOXO3a and AP-1*. Treatment with TRF has shown to modulate the expression of antioxidant associated genes, IGF-1/ PI3K/ Akt associated genes, DNA damage and cell proliferation genes.

Conclusion:
Our results confirmed that the expression of these genes was altered during cells senescent. Treatment with TRF however modulated these changes indicating the potential protective mechanism in delaying and preventing cellular aging.

Keywords:
Tocotrienol-rich fraction, senescence associated genes, cellular aging